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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/722,292

11/25/2003

Richard A. Shimkets

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10/02/2006

MERCHANT & GOULD PC

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MINNEAPOLIS, MN 55402-0903

EXAMINER

WHITEMAN, BRIAN A

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 10/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/722,292

Applicant(s)

SHIMKETS ET AL.

Examiner

Brian Whiteman

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 14 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 50-66 is/are pending in the application.
- 4a) Of the above claim(s) 54-61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 50-53 and 62-66 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 November 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 5/10/06, 12/24/03, 9/8/06
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Notice to Comply/SEQ.

### **DETAILED ACTION**

Claims 50-66 are pending.

The addition of claims 50-66 and the cancellation of claims 1-49 in paper filed on 7/14/06 is acknowledged.

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be to directed to Brian Whiteman, Art Unit 1635.

The examiner has considered the European Search Report, but did not initial it on the IDS submitted on 9/8/06 because it is not considered a published document.

### ***Election/Restrictions***

Applicant's election with traverse of Group VII (CH-9, SEQ ID NO: 9 (claims 50-66)) in the reply filed on 7/14/06 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden to search more than one single species of the polynucleotide and ligand in the method as claimed by applicant (See 37 CFR 1.141). This is not found persuasive because a nucleic acid encoding CH-1 through CH-9 are not species. As stated in the election/restriction, this was not a species election. Each nucleic acid comprises a distinct structure and mode of operation. Thus, it would be an undue burden to search and examine an agent that inhibits expression of the CHAG polynucleotide comprising SEQ ID NOs: 1-9.

The requirement is still deemed proper and is therefore made FINAL.

NOTE: There is an improper Markush group in Claim 50. Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature essential to that utility. See *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980). The ligands (protein, a fragment of the protein comprising a domain of the protein, a nucleic acid encoding the protein or fragment selected from CH-9 in claim 50 does not share a common utility and do not share a substantial structural feature.

A protein and a fragment of the protein comprising a domain of the protein and CH-1 through CH-8 in claim 50, SEQ ID NOs: 1-8 in claim 51, and claims 54-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/14/06.

In view of the addition of new claims 50-66, a species election is further required for the species in claim 53.

During a telephone conversation with Katherine Kowalchuk on 7/19/06 a provisional election was made with traverse to prosecute the species an antisense RNA, claim 53.

Affirmation of this election must be made by applicant in replying to this Office action. A catalytic RNA, a ribozyme, a chimeric RNA-DNA analogue in claim 53 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

However, upon further consideration the election of species for the antisense nucleic acid in instant claim 53 is moot and the non-elected species will be rejoined and examined with the

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elected species. Thus, the election of species is moot and the applicant is not required to affirm the election of species.

### ***Oath/Declaration***

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the new claims contain new matter that was not in the parent application(s). See MPEP 602.05(a).

### ***Priority***

The cross-reference to parent applications on page 1 needs updated.

In view of the new matter rejection, the relationship of this case to the parent application 09/554,169 may be improper.

This application repeats a substantial portion of prior Application No. 09/554,168, filed 8/21/00, and adds and claims additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/554,169, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Instant claims 51-53 and 62-64 do not have written support under 112 first paragraph in '169.

Furthermore, the new claims were filed after the instant application was filed. Thus, the instant claims 51-53 and 62-64 only enjoy priority to the amendment filed on 7/14/06.

### ***Specification***

This application contains sequence disclosures that are encompassed by the definition for nucleotide sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements for Patent Applications Containing Nucleotide Sequence Disclosures.

Figures 2-10 (panel B) contain a nucleotide sequence that is not listed in the CRF.

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A complete response to the instant office action must include a response to the sequence compliance notification.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-53 and 62-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

**New matter rejection**

The new claims were filed on 7/14/06. Applicants cite support for the new claims. However, the support cited in the instant specification does not support the new claims. Therefore, there does not appear to be a written description of the new claims in the application as filed. See MPEP § 2163.06. Applicants cite page 49, line 13 to page 50, line 18. However, page 49, line 13 is directed to immunoassays. Page 49, line 14 to page 50, line 3 is directed to detection expression of CHAG genes using techniques known in the art including Southern hybridization and Northern hybridization (these hybridizations require a probe to the CHAG gene). Page 50, line 4 to line 18 is directed to assaying an unspecified therapeutic in cultured cells that exhibit an indicator of a cardiac hypertrophy and in vitro models for cardiac

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hypertrophy. Applicants cite page 39, line 25 to page 43, line 11. Pages 39-43 are directed to therapeutic utilization of CHAG antisense nucleic acids. Applicants cite page 46, line 18 to page 48, line 18. Pages 46-48 are directed to in vitro screening methods for CHAG modulators to detect molecules that specifically bind to CHAG nucleic acids, proteins or derivatives. It appears that the new claims are based on picking and choosing from the disclosure on several pages in the specification, wherein each part of the specification is directed to different embodiments. The specification provides support for a method of identifying a candidate in cultured cells in vitro as set forth in instant claims 65 and 66. Thus, nothing in the specification would lead one to the particular combination set forth in the new claims and claims dependent therefrom. See *Purdue Pharma L.P. v. Faulding Inc.* 230 F.3d 1320, 1326, 56 USPQ2d 1481, 1486 (Fed. Cir. 2000) noting that “with respect In re Ruschig 379 F.2d 990, 154 USPQ 118 (CCPA 1967) that Ruschig makes clear that one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say “here is my invention.” In order to satisfy written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure.” This is the case here, the applicant did not disclose using a CHAG polynucleotide comprising SEQ ID NO: 9 with a candidate agent (antisense agent) to identify if the agent inhibits CHAG expression in a genus of cells.

“It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose.” *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961, 1966 (CAFC 1997).



Claims 50, 51, and 63-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 50, as best understood, is readable on a genus of molecules that bind to a nucleic acid encoding CH-9 or fragment thereof, wherein the genus of molecules is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 51 and 63-66, as best understood, is readable on a genus of candidate agents that inhibits CHAG (SEQ ID NO: 9) expression, wherein the genus of candidate agents is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 (Fed Cir. 1991), clearly states that:

The applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for

purposes of the 'written description' inquiry, *whatever is not claimed.*" *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The instant specification contemplates a genus of molecules that bind to CHAG nucleic acids. The elected invention is directed to a molecule that binds to a ligand (nucleic acid encoding CH-9 (SEQ ID NO: 9) or a fragment). The specification further contemplates using the CHAG nucleic acids to produce proteins that bind to the molecule. However, the elected invention is directed to an agent that inhibits expression of a CHAG polynucleotide comprising CH-9 (SEQ ID NO: 9). The term CH-9 and fragment of CH-9 in claim 50 is broader than a CHAG polynucleotide comprising SEQ ID NO: 9. Page 9 of the instant specification contemplates CH-9, as well as derivatives and analogs thereof and CH-9 has nucleotide sequence homology to mouse and human zyxin. Page 9 further recites: The invention relates to derivative and analogs of CH-9 proteins that are functionally active, i.e., they are capable of displaying one or more functional activities associated with a full-length (wild-type) protein. With respect to claims 50 and 63-66, there is a variation among species embraced by the claimed genus of molecules. For examples, the genus embraces nucleic acid encoding genomic DNA encoding CH-9 from human, rat, mouse, rabbit, bear, monkey, etc. In addition, the instant specification does not disclose which nucleotides are considered essential for binding a molecule to the nucleic acid or fragment thereof. Furthermore, the instant specification does not disclose how to make the genus of agents and/or molecules. The elected invention embrace making and using dominant negative nucleic acids and antisense nucleic acid molecules, which interfere with the

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function of the CH-9 nucleic acid such as DNA replication, transcription, translocation of the CH-9 to the site of protein translation, translation of protein from the CH-9 RNA, splicing of the CH-9 to yield one or more mRNA species, or catalytic activity which may be engaged in or facilitated by the CH-9. One skilled in the art can envision a sequence that hybridizes to a CHAG polynucleotide comprising SEQ ID NO: 9 and would be able to determine if the sequence had a function that was considered essential for the claimed genus of molecules.

However, there is a variation among species of the claimed genus of molecules. For example, the genus of molecules embraces oligonucleotides that bind to introns and cap structures that are neither disclosed in the specification nor the prior art. In addition, the skilled artisan understands that human CH-9 gene with polymorphisms are embraced by the claimed genus that are not disclosed in the instant specification or prior art. Furthermore, the specification does not disclose how to make a sufficient number of species to represent the genus of claimed molecules. The mere contemplation of the claimed genus of molecules in the specification is not sufficient to support the present claimed invention directed to a genus of molecules.

It is apparent that on the basis of applicants' disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of small interfering molecules as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of agents and/or molecules that must exhibit the disclosed biological functions as contemplated by the claims.

The mere contemplation of the claimed genus in the specification is not sufficient to support the present claimed invention directed to a genus of molecules and/or agents that specifically bind to a nucleic acid encoding CH-9. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of molecules and/or agents that must possess the biological properties as contemplated by applicants' disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CAFC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of agents and/or molecules that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 50-53 and 62-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a candidate agent that inhibits CHAG gene expression comprising contacting an in vitro cell comprising a CHAG polynucleotide comprising SEQ ID NO: 9 with a candidate agent and determining whether candidate agent inhibits expression of the CHAG polynucleotide, does not reasonably provide enablement for a method of identifying a candidate agent that inhibits CHAG gene expression comprising contacting a genus of cells comprising a CHAG polynucleotide comprising SEQ ID NO: 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors as enumerated *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), are considered when making a determination that a disclosure is not enabling: the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples and the quantity of experimentation needed to make the invention based on the content of the disclosure.

The claimed invention reads on a method of identifying a genus of candidate agents that inhibits CHAG gene expression comprising contacting a nucleic acid consisting of a CHAG polynucleotide comprising SEQ ID NO: 9. The method further comprises using a genus of cells. Thus, the claims are considered broad.

Furthermore, with respect to claims 50-53 and 62-64, the claims encompass a method of identifying a genus of candidate agents, wherein the method does not/does require a cell. The

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specification provides sufficient guidance for one skilled in the art to use the method in a cell in vitro. However, the specification fails to provide sufficient guidance or evidence for one skilled in the art to use the method not in a cell or a cell in vivo. The teachings in the specification are directed to using the claimed method in vitro.

The applicants study gene expression occurring during pressure overload hypertrophy using QEA to identify expression differences in a rat surgical model of pressure overload induced cardiac hypertrophy (pages 58-71). The instant specification does not provide any working examples of the claimed method.

Problems related to *in vivo* use of nucleic acids were well known in the art at the time of invention and persist to the present day; see Opalinska et al. (Nature Reviews Drug Discovery 2002). Such problems include the inability to specifically deliver an effective concentration of a nucleic acid to a target cell, such that a target gene is inhibited to a degree necessary to result in a measurable or therapeutic effect.

Opalinska et al. state on page 511

“[I]t is widely appreciated that the ability of nucleic-acid molecules to modify gene expression *in vivo* is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells and identification of sequence that is accessible to hybridization in the genomic DNA or RNA” and in column 2 of the same page, “Another problem in this field is the limited ability to deliver nucleic acids into cells and have them reach their target. Without this ability, it is clear that even an appropriately targeted sequence is not likely to be efficient. As a general rule, oligonucleotides are taken up primarily through a combination of adsorptive and fluid-phase endocytosis. After internalization, confocal and electron microscopy studies have indicated that the bulk of the oligonucleotides enter the endosome-lysosome compartment, in which most of the material becomes either trapped or degraded.”

Given this unpredictability, the skilled artisan would require specific guidance to practice the claimed methods *in vivo* in all organisms, with a resultant inhibition of gene expression, as claimed. Often formulations and techniques for delivery *in vitro* (cell culture) are not applicable *in vivo*; due to differences in the physiological conditions of a cell *in vitro* versus *in vivo*, the

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uptake and biological activity observed *in vitro* would not predictably translate to *in vivo* results. Given these teachings, the skilled artisan would not know *a priori* whether introduction of nucleic acids *in vivo* by the broadly disclosed methodologies of the instant invention, would result in the nucleic acid reaching the proper cell in a sufficient concentration and remaining for a sufficient time to provide successful inhibition of expression of a target gene. In fact, the state of the art is such that successful delivery of nucleic acid sequences *in vivo* or *in vitro*, such that the nucleic acid provides the requisite biological effect to the target cells/tissues/organs, must be determined empirically.

The specification does not provide the guidance required to overcome the art-recognized unpredictability of using nucleic acids for *in vivo* applications. The teaching of the prior art does not provide that guidance. Thus, to the extent the claims fail to recite distinguishing features to commensurate with the level of guidance presented, the claims are not considered enabled.

In conclusion, the instant specification and claims coupled with the art of record, at the time the invention was made, provide enablement for a method of identifying a candidate agent that inhibits CHAG gene expression comprising contacting an *in vitro* cell comprising a CHAG polynucleotide comprising SEQ ID NO: 9 with a candidate agent and determining whether candidate agent inhibits expression of the CHAG polynucleotide, and not for the full scope of the claimed invention. However, the rest of the disclosure encompassing a genus of methods of identifying a candidate agent is not considered enabled for the reasons set forth above. Given that inhibiting gene expression *in vivo* and identifying a genus of candidate agents *in vivo* was unpredictable at the time the invention was made, and given the lack of sufficient guidance for producing the claimed method in a cell *in vivo* or not a cell, one skilled in the art would have to

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engage in a large quantity of undue experimentation in order to practice the full scope of the claimed invention based on the applicant's disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 50-53 and 62-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 50-53 and 62-63 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: where the contacting step is taking place, e.g., test tube, microtiter plate, a cell, etc.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of



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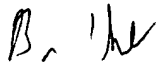
such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman



BRIAN WHITEMAN  
PATENT EXAMINER

<b>Notice to Comply</b>	<b>Application No.</b> 10/722,292	<b>Applicant(s)</b> SHIMKETS et al.	
	<b>Examiner</b> B. Whiteman	<b>Art Unit</b> 1635	

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: See office action, heading specification.

**Applicant Must Provide:**

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the specification.**
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510

For CRF Submission Help, call (571) 272-2501/2583.

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